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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/335,956	06/18/99	WARD D	IGI-001CN3

ID

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HM22/0601

EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
1655	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/335,956	Applicant(s) WARD ET AL.	
	Examiner BJ Forman	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *18 June 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Receipt of a substitute specification, copies of the amendments to the original specification and a substitute specification showing the amendments is acknowledged.

Claims 1-18 are pending in the instant application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-6 are indefinite because they are drawn to methods for labeling chromosomes but the claims do not recite method steps for labeling. It is suggested that the claims be amended to insert "labeled" before "probes" and to recite positive, active method steps e.g. hybridizing, detecting

b. Claims 3-6 are indefinite because they are drawn to methods for decoration of chromosomes but the claims do not recite method steps for decorating. It is suggested that the claims be amended to recite positive, active method steps e.g. hybridizing, detecting.

c. Claims 7 & 8 are indefinite because the claims are drawn to a method of assessing, but the claim does not recite positive active method steps for assessing. It is suggested that the claim be amended to recite positive, active method steps.

Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter the claims encompass

as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

d. Claims 9-12 are indefinite because it is unclear how step b) "detecting labeled human DNA..." relates to the claimed method for "detecting chromosome aberrations". It is suggested that the claims be amended to clarify the relationship e.g. recite at the end of claim 9 "thereby detecting chromosome aberrations." The claims are further indefinite because it is unclear whether the chromosomal aberrations being detected are the aneuploid aberrations present in the aneuploid cells or whether other aberrations are being detected. It is suggested that the claims be amended to clarify what aberrations are being detected.

e. Claims 13-15 are indefinite because it is unclear how step b) "detecting labeled DNA..." relates to the claimed "method of detecting in a sample numerical alterations in a human chromosome". It is suggested that the claims be amended to clarify the relationship and to recite a method step for detecting numerical alterations.

f. Claims 13-15 are indefinite in step 2) for the recitation "the selected chromosome" because the recitation lacks proper antecedent basis in the preamble of Claim 13. It is suggested that Claim 13 be amended in the first line of step 2) to delete "the" and insert "a".

g. Claims 13-15 are indefinite in line 3 of step 2) because words are missing and/or misplaced and because step 2) contains two steps labeled b). It is suggested that Claim 13 be amended to recite step 2) as originally filed i.e. in lines 3-4 of step 2) delete; "occur; and b) detecting labeled DNA de-selected chromosome hybridization of complementary nucleic".

h. Claim 16 is indefinite because it is unclear how step b) "detecting labeled human chromosome-specific DNA..." relates to the claimed method for "determining over-representation or under-representation..". It is suggested that the claims be amended to clarify the relationship and to recite method steps for determining over-representation or under-representation.

i. Claims 17 & 18 are indefinite because it is unclear how step b) "detecting complexes formed" relates to the claimed method for "identifying chromosome-specific DNA...". It is suggested that the claims be amended to clarify the relationship and to recite method steps for detecting complexes.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 1-9, 13-15 & 17 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Gray et al. (U.S. Patent No. 5,447,841, files 14 December 1990).

Regarding Claims 1 & 2, Gray et al. disclose a method of labeling individual mammalian i.e. human chromosomes (Column 15, line 58-Column 16, line 57) in mitotic i.e. metaphase cells and interphase cells by in situ hybridization (Column 4, lines 57-62) with chromosome-specific probes (Column 16, lines20-23) to thereby produce a chromosome-specific signal (Column 16, lines 41-47)

Regarding Claim 3, Gray et al disclose the labeling produces highly specific decoration of an individual target chromosome i.e. 21 (Column 16, lines 45-57 and Fig. 1).

Regarding Claim 4, Gray et al. disclose the DNA probes are specific DNA inserts purified from a chromosome-derived recombinant DNA library (Column 14, lines 29-49).

Regarding Claims 5 & 6, Gray et al. disclose the labeled DNA probes are labeled with one member of a specific binding pair i.e. biotin (Column 14, lines 49-52).

Regarding Claim 7, Gray et al disclose a method of assessing chromosome aberrations in human cells (Column 5, lines 20-34) by chromosomal in situ suppression hybridization wherein non-specific hybridization is suppressed (Column 4, lines 47-56).

Regarding Claim 8, Gray et al disclose a method of assessing chromosome aberrations in human cells wherein the human cells are metaphase and interphase cells (Column 5, lines 29-33).

Regarding Claim 9, Gray et al. disclose the method for detecting chromosomes aberrations in human aneuploid cells (Column 5, lines 6-22 and Claim 9) comprising, combining human cells treated so as to render nucleic acid sequences available for hybridization (Column 15, line 66-Column 16, line 16) and a hybridization mixture comprising labeled human DNA derived from a specific chromosome i.e. 21, competitor DNA i.e. human genomic DNA and non-human genomic DNA i.e. lambda DNA under conditions appropriate for hybridization (Column 16, lines 16-20 and 30-41) and detecting labeled human DNA derived from the specific chromosome hybridized to nucleic acid sequences from the cells (Column 16, lines 41-57 and Fig. 1).

Regarding Claim 13, Gray et al. disclose a method for detecting in a sample numerical alterations in a human chromosome in the sample (Column 5, lines 6-22 and Claim 6) comprising, combining human cells treated so as to render nucleic acid sequences available for hybridization (Column 15, line 66-Column 16, line 16) and a hybridization mixture comprising labeled human DNA derived from a specific chromosome i.e. 21, competitor DNA i.e. human genomic DNA and non-human genomic DNA i.e. lambda DNA under conditions appropriate for hybridization (Column 16, lines 16-20 and 30-41) and detecting labeled DNA derived from the selected chromosome hybridized to nucleic acid sequences present in the sample (Column 16, lines 41-57 and Fig. 1).

Regarding Claim 14, Gray et al. disclose the method of Claim 13 wherein the selected human chromosome is number 21 (Column 16, lines 21-23 and Claim 10)

Regarding Claim 15, Gray et al. disclose the method of Claim 13 wherein the selected human chromosome is number 21 and the labeled human DNA derived from the selected chromosome is DNA inserts purified from a chromosome-derived recombinant DNA library (Column 14, lines 31-35).

Regarding Claim 17, Gray et al. disclose a method of identifying chromosome-specific DNA present in a selected mammalian chromosome (Column 5, lines 6-22 and Claim 1) comprising combining the selected chromosome, labeled DNA fragments derived from the selected mammalian chromosome i.e. biotin-labeled human chromosome 21-specific DNA, competitor DNA i.e. human genomic DNA and carrier DNA i.e. lambda DNA (Column 16, lines 16-20) under conditions appropriate for hybridization of complementary nucleic acid sequences to occur (Column 16, lines 30-41) to thereby form a complex of DNA fragments bearing a detectable label with the selected mammalian chromosome and detecting the complexes formed (Column 16, lines 41-57 and Fig. 1).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (U.S. Patent No. 5,446,841, filed 14 December 1990) as applied to Claim 9 above.

Regarding Claims 10-12, Gray et al. disclose the method for detecting chromosomes aberrations in human aneuploid cells (Column 5, lines 6-22 and Claim 9) but they do not teach the method wherein the cells are human tumor cells (Claim 10) wherein the human tumor cells are selected from the group consisting of metaphase, prophase and interphase cells (Claim 11) and wherein the tumor cells are human glioma (Claim 12). However, Gray et al. teach the method for detecting chromosomal abnormalities is applicable to cancer diagnosis (Column 5, lines 33-35). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method of Gray et al. with the teachings of Gray et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the Gray et al. method for detecting chromosomal abnormalities to tumor cells because tumor cells which were known to contain chromosomal abnormalities for the expected benefit of rapid and highly sensitive detection of tumor causing chromosomal abnormalities as taught by Gray et al. (Column 5, lines 29-35).

8. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (U.S. Patent No. 5,446,841, filed 14 December 1990). Gray et al. teach a method for determining over-representation or under-representation of a selected chromosome (Column 5, lines 6-22 and Claim 6) comprising, combining human cells treated so as to render nucleic acid sequences available for hybridization (Column 15, line 66-Column 16, line 16) and a hybridization mixture comprising labeled human DNA derived from a specific chromosome i.e. 21, competitor DNA i.e. human genomic DNA and non-human genomic DNA i.e. lambda DNA under conditions appropriate for hybridization (Column 16, lines 16-20 and 30-41) and detecting labeled human chromosome-specific DNA fragments hybridized to nucleic acid sequences from the cells (Column 16, lines 41-57 and Fig. 1). Gray et al. do not teach the cells are human tumor cells. However, Gray et al. teach the method for determining over-

representation or under-representation of a selected chromosome is applicable to cancer diagnosis (Column 5, lines 33-35). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method of Gray et al. with the teachings of Gray et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the Gray et al. method for detecting chromosomal abnormalities to tumor cells because tumor cells were known to contain chromosomal over and/or under-representation for the expected benefit of rapid and highly sensitive detection of tumor causing chromosomal abnormalities as taught by Gray et al. (Column 5, lines 29-35).

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (U.S. Patent No. 5,447,841, files 14 December 1990) as applied to claim 17 above. Gray et al. disclose the method of Claim 18 wherein the repetitive sequences are removed from the chromosome-specific DNA (Column 8, lines 45-53) but they do not teach the complexes formed by hybridization with chromosome-specific DNA is isolated from the remaining substances. However, it was known and routinely practiced in the art to separate complexed DNA. It would have been prima facie obvious to one of ordinary skill in the art to modify the method of Gray et al. with routinely practiced procedures to obtain the claimed invention because one of skill in the art would have been motivated with a reasonable expectation of success to separate the complexed DNA for the obvious benefit of analyzing the DNA of interest in isolation i.e. without extraneous cross reacting or contaminating substances.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8742 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
June 1, 2000